

1
ould
B1

distinguishing red blood cells from other cellular particles, prior to the red blood cell analysis are also disclosed. Red blood cells are passed through a beam of light in single file at a selected wavelength, obtaining an initial cytogram by means of the resultant magnitude of one light loss signal and one forward angle light scatter signal at a selected angular interval and a third side angle light scatter or two forward angle light scatter signals at a selected angular intervals and a third side-angle light scatter signal, projecting the cytogram, point by point, onto a pre-calibrated 3-dimensional surface containing grid lines of volume and hemoglobin concentration and determining accurate values of cell volume and hemoglobin concentration.

2) Please amend the specification as follows:

At page 8, line 28, please delete - "sphaered"- and insert thereof - "sphered"-.

At page 8, line 26, please delete - "vey" - and insert thereof - "very" -.

REMARKS

Claims 1-21 are pending and currently under examination. Claims 1-8 and 12-21 are rejected, and claims 9-11 are objected to.

Objections to Specification

1) The abstract of the disclosure was objected to for being too short and having little indication of what is inventive. Applicants have replaced the previous Abstract (on page 28, lines 1-4) with a new Abstract that provides a better description of the presently claimed invention.

2) The disclosure was objected to for informalities in pages 8 and 26. Applicants have amended the typographical errors in the specification to conform to those words suggested by the Examiner and originally intended by the Applicants.

Applicants respectfully request that the objections be withdrawn.

Rejections under 35 U.S.C. § 103(a)

1) Claims 1-4, 12-15 and 19-21 stand rejected under 35 U.S.C. § 103 as being obvious over Tycko, US Patent 5,194,909 (hereinafter “ ‘909 patent”) in view of Kim *et al.*, US Patent 5,559,037 (hereinafter “ ‘037 patent”). Applicants respectfully traverse the rejection.

Effective November 29, 1999, subject matter which was prior art under former §103 via § 102(e) is now disqualified as prior art against the claimed invention if that subject matter and the claimed invention, “were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person”. MPEP 706.02(l)(1). To establish common ownership Applicant must submit a clear and conspicuous statement of common ownership at the time the invention was made. Applicants respectfully submit said evidence of common ownership in a separate document included in the present response. In the instant case, the subject matter of the ‘037 patent and the claimed invention, were commonly owned by the same company at the time the invention of the presently pending application was made, thus disqualifying the ‘037 patent as prior art cited against the invention. This leaves Tycko as the only piece of prior art. Applicants respectfully assert that Tycko’s patent alone does not teach nor suggest the subject matter of the present invention.

Tycko teaches an apparatus and method for measuring volume and hemoglobin concentration of individual red blood cells using the signals detected by a scattered light detector and a resistance pulse-sizing aperture. The present invention claims a method and apparatus for three-dimensional optical analysis of red blood cells on cell-by-cell basis for volume, hemoglobin concentration, cell-shape abnormality, immaturity (% reticulocytes and their volume and hemoglobin concentration by means of a fourth fluorescence signal), and simultaneous analysis of white blood cell differential using the same optical bench plus continuous monitoring of the system standardization while blood samples are being analyzed.

Tycko only teaches the use of two variables, V and SL, in two dimensions. V values from the pulse sizing aperture and SL values from forward scatter signal heights.

Fig 4 of the '909 patent represents plots from SL angular interval between $\theta_L = 8.5^\circ$ and $\theta_H = 25^\circ$ and Fig 5 represents plots from SL angular interval between $\theta_L = 6^\circ$ and $\theta_H = 10^\circ$. In Figures 4 and 5, Tycko is simply showing that two different angular intervals generate different forward light scatter patterns and the choice of the former (Fig 4 plot) generate a better linearity in HC measurement. Tycko does not use the four features of the present invention mentioned above. Additionally, Tycko's patent does not teach the simultaneous determination of red blood cell properties, normal/abnormal cell shape and maturity, and the determination of immature red blood cells (reticulocytes) and white blood cell differential analysis as in the present invention. In view of the above arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-4, 12-15 and 19-21 under §103.

2) Claims 5-8 and 16 stand rejected under 35 U.S.C. § 103(a) as obvious over Tycko as modified by the '037 patent as applied to claim 1 in further view of Kim, US 5,691,204 (hereinafter "'204 patent").

Applicants respectfully traverse the rejection for the reasons stated in section (1). Furthermore, the subject matter of the '204 patent and the claimed invention were commonly owned at the time the claimed invention was made. A statement establishing evidence of common ownership of the subject matter of the present invention at the time the invention was made, and the subject matter of the '037 and '204 patents is submitted.

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 5-8 and 16 under 35 U.S.C. § 103(a).

3) Claims 17 and 18 stand rejected under 35 U.S.C. § 103(a) as obvious over Tycko as modified by the '037 patent as applied to claim 13 and further in view of Kirchanski *et al.*, US Patent 4,882,284 (hereinafter "'284 patent").

For the reason stated in sections 1 and 2, the '037 patent is disqualified as prior art, leaving only Tycko and Kirchanski *et al.* as the references to be considered to establish a prima facie case of obviousness under § 103(a). The combination of these two references does not render the claimed invention obvious.

Tycko teaches an apparatus and method for measuring volume and hemoglobin concentration of individual red blood cells using the signals detected by a scattered light detector and a resistance pulse-sizing aperture.

Kirchanski *et al.* teaches the discrimination of white blood cells from red blood cells in unlysed blood using fluorescent dyes stimulated by a red light laser. The discrimination is obtained because of the greater fluorescence developed by the white blood cells compared to the red blood cells. Subtypes of white blood cells can be detected because of their different membrane properties, nuclear structure, size and internal granularity, giving rise to different signals of light scattering and fluorescence. Unlike white blood cells, red blood cells do not contain nucleus (except in the case of severe anemia), granules, pseudopods or cytoplasmic organelles. Red blood cells are primarily made of cell membrane and hemoglobin solution inside the membrane. Thus, Kirchanski's teachings in the prior art do not apply to red blood cell analysis.

Neither Tycko nor Kirchanski teach, as the instant invention does, a method and apparatus for the simultaneous determination of red blood cell properties including volume, hemoglobin content, normal/abnormal cell shape and maturity, plus determination of immature red blood cells (reticulocytes) and simultaneous white blood cell differential analysis using the same optical bench. The measurements of the present invention are achieved by using a pre-calibrated three-dimensional surface constructed from three different angle optical signals and a fourth fluorescence signal to identify immature red blood cells prior to subjecting each cell to the 3D surface analysis.

Tycko and Kirchanski combined fail to teach the simultaneous determination of RBC characteristics and the WBC differential analysis. Kirchanski does not disclose any information on RBC differential analysis. Additionally, Kirchanski fails to teach the use of visible wavelength light source that would permit the inclusion of more sensitive fluorescent dyes for nuclear stain that would allow an easier identification and separation of immature red blood cells and does not use a pre-calibrated three-dimensional surface.

In view of the above discussion, Applicants respectfully submit that Tycko and Kirchanski individually do not provide a motivation to combine both references and, additionally, a combination of Tycko and Kirchanski does not generate all the elements of the present invention.

Therefore, Applicants respectfully request that the rejection of claims 17 and 18 be reconsidered and withdrawn.

Allowable subject matter

Examiner argues that claims 9-11 are objected to as being dependent upon rejected base claim, but would be allowable if rewritten in independent form. Applicants respectfully submit that in view of the above discussion, the rejections be withdrawn and that claims 9-11 be allowed in their present format.

CONCLUSION

Applicants respectfully submit that the claims comply with all the requirements for patentable subject matter over the art. Accordingly a Notice of Allowance is respectfully requested.

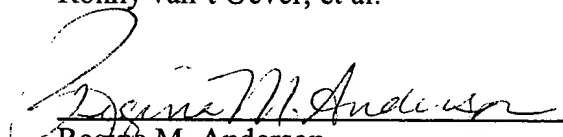
If the Examiner notes any further matters that the Examiner believes to be expedited by a telephone interview, the Examiner is requested to contact the undersigned.



23492

ABBOTT LABORATORIES
Telephone: (847) 937-8284
Facsimile: (847) 938-2623

Respectfully submitted,
Ronny van't Oever, et al.


Regina M. Anderson
Registration No. 35, 820
Attorney for Applicants